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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/894,912	06/28/2001	Y. Tom Tang	30266/37260A	4685

4743 7590 04/19/2004

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/894,912	TANG ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *62-65 and 74-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *62-65 and 74-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 22 December 2003 has been entered in full. Claims 62, 64-65, and 74-75 are amended. Claims 1-62 and 66-73 are cancelled. Claims 76-77 are added.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 62-65 and 74-77 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objections to the specification at pg 3-4 of the previous Office Action (18 June 2003) are *withdrawn* in view of the amended specification (22 December 2003).

2. The rejection of claims 62-65 and 74-75 under 35 U.S.C. § 112, first paragraph (enablement), as set forth at pg 4-8 of the previous Office Action (18 June 2003) is *withdrawn in part* in view of Applicant's persuasive arguments and the amended claims (22 December 2003). Please see section on 35 U.S.C. § 112, first paragraph, below. It is noted by the Examiner that Examples 6 and 17 of the specification (pg 168 and 185-186) indicate that the SCR-1 polypeptide of instant application promotes proliferation and survival of mouse hematopoietic stem cells.

3. The rejection of claim 62 under 35 U.S.C. § 112, first paragraph (written description) as set forth at pg 8-10 of the previous Office Action (18 June 2003) is *withdrawn* in view of the amended claim (22 December 2003).

4. The rejections to claims 62-65 and 74-75 under 35 U.S.C. § 112, second paragraph, as set forth at pg 11 of the previous Office Action (18 June 2003) are *withdrawn* in view of the amended claims (22 December 2003).

Claim Rejections - 35 USC § 112

5. Claims 62-65 and 74-77 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an ex vivo method of promoting proliferation or maintaining survival of a hematopoietic stem cell or hematopoietic progenitor cell comprising contacting said cell with an amount of a polypeptide, wherein said polypeptide comprises an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID NO: 13, 32, or 34 or the mature protein coding portion thereof and exhibits stem cell growth factor activity, *does not* reasonably provide enablement for an ex vivo method of promoting proliferation or maintaining survival of a stem cell or germ cell comprising contacting said cell with an amount of a polypeptide, wherein said polypeptide comprises an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID NO: 13, 32, or 34 or the mature protein coding portion thereof and exhibits stem cell growth factor activity. The specification is also only enabling for an ex vivo method of promoting proliferation or maintaining survival of a stem cell comprising contacting said cell with an amount of a polypeptide, wherein the polypeptide is encoded by a polynucleotide that hybridizes to the complement of the nucleotide sequence of SEQ ID NO: 12, or the mature protein coding portion thereof, under the following stringent conditions: a final wash of 0.1x SSC/0.1% SDS at 68°C. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make

and use the invention commensurate in scope with these claims. The basis for part of this rejection is set forth at pg 4-8 of the previous Office Action (18 June 2003).

The claims also recite that the cell is a primordial germ cell, germ line stem cell, embryonic stem cell, hematopoietic stem cell, hematopoietic progenitor cell, pluripotent cell, or totipotent cell.

Applicant's arguments (22 December 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that the specification supports the proliferation or survival of stem cells *in vivo*. Applicant argues that the experiments in Example 17 demonstrate murine SCF-1 supports stem cell proliferation *in vivo* in irradiated mice. Applicant also indicates that in order to expedite prosecution, the claims have been amended to be directed to *ex vivo* methods.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, claim 65 still encompasses a method of promoting proliferation of a stem cell or germ cell *in vivo*. This claim has not been amended to recite an *ex vivo* method. Furthermore, Example 17 of the specification teaches that hematopoietic cells co-cultured with AGM-s3-A7 stromal cells transduced with SCR-1 gene are transplanted into irradiated mice (pg 185). The specification teaches that a significant high proportion of cells derived from the cultured cells are detected in myeloid and lymphoid cells in the peripheral blood (pg 186, second full paragraph; Figure 7). However, the specification does not teach any methods or working examples that indicate that administration of the SCR-1 polypeptide itself to a subject. There is little guidance in the specification or working examples that indicate the stem cell growth factor-like polypeptide of SEQ ID NOs: 13, 32, and 34 is able to promote cell proliferation or survival *in*

vivo. Undue experimentation would also be required of the skilled artisan to determine the optimal dosage, duration, and route of administration of the stem cell growth factor-like polypeptide if administered to cells *in vivo*.

(ii) The specification of the instant application teaches that mouse stem cells are co-cultured with stem cell growth factor-like polynucleotide transduced stromal cells (Example 6, pg 168; Example 17, pg 185-186). The specification also teaches that CD34+ hematopoietic stem cells are cultured with purified stem cell growth factor-like protein and other hematopoietic cytokines (Example 7, pg 168-169). However, there are no methods or working examples that indicate all possible stem cells and germ cells are contacted with the SCR-1 polypeptide of SEQ ID NOs: 13, 32, or 34. Undue experimentation would be required of the skilled artisan to promote the proliferation of all possible stem and germ cells (such as neural stem cells, epidermal stem cells, primordial germ cells, germ line stem cells, embryonic stem cells, pluripotent cells, or totipotent cells) by contacting the cells with a polypeptide having an amino acid sequence of SEQ ID NO: 13, 32, or 34. The specification discloses that the term primordial germ cells (PGCs) "refers to a small population of cells set aside from other cell lineages particularly from the yolk sac, mesenteries, or gonadal ridges during embryogenesis that have the potential to differentiate into germ cells and other cells" (pg 25, lines 16-20). The specification teaches that the term germ line stem cells (GSCs) "refers to stem cells derived from primordial stem cells that provide a steady and continuous source of germ cells for the production of gametes" and that the term embryonic stem cells "refers to a cell which can give rise to many differentiated cell types in an embryo or an adult, including the germ cells" (pg 25, lines 21-29). The specification discloses that the term totipotent "refers to the capability of a cell to differentiate into all of the cell types

of an adult organism" and that the term pluripotent "refers to the capability of a cell to differentiate into a number of differentiated cell types that are present in an adult organism" (pg 25, lines 30-31 through pg 26, lines 1-4). Additionally, stem cells are defined in the art as precursor cells with the capacity for both replication and differentiation. The specification of the instant application only teaches that hematopoietic stem and progenitor cells proliferate in response to contact with the polypeptide of SEQ ID NOs: 13, 32, or 34. Undue experimentation would be required of the skilled artisan to isolate all possible stem and germ cells and contact the cells with the SCR-1 polypeptide of the instant application to promote proliferation or maintain survival. One skilled in the art would not be able to predict that all stem cells and germ cells would be responsive to the SCR-1 polypeptide of the instant application since the broad genus of stem and germ cells recited in the claims are present at varied stages and locations in an organism. The cells may also only be responsive to specific cytokines and growth factors.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to support the proliferation of all possible stem and germ cells *in vitro* and *in vivo* by contacting the cells with the polypeptide of amino acid sequence SEQ ID NO: 13, 32, or 34; to determine the quantity of stem cell growth factor-like protein to be administered *in vivo*, the most effective administration route, and the duration of the treatment; the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of the effects of the stem cell growth factor-like protein *in vivo* and on all possible stem cells and germ cells, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

BEB
Art Unit 1647
15 April 2004